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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/436,076	11/08/1999	DENISA D. WAGNER	10861/011003	6116

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EXAMINER
GAMBEL, PHILLIP

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 07/14/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/436,076	WAGNER ET AL.	
	Examiner	Art Unit	
	Phillip Gambel	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☑ Responsive to communication(s) filed on 5/4/04.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☑ Claim(s) _____ is/are pending in the application. 40, 41, 49-52, 59, 60, 73

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☑ Claim(s) _____ is/are rejected. 40, 41, 49-52, 59, 60, 73

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1)☒ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4)☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other: _____.

DETAILED ACTION

1. Applicant's Brief on Appeal, filed 5/4/04, is acknowledged.

Upon reconsideration, New Grounds of Rejection have been set forth to address the claim limitation restenosis.

Claims 40-41, 49-52, 59-60 and 73 are pending

Claims 1-39, 42-48, 53-58, 61-72 and 74 have been canceled previously.

2. The text of those sections of Title 35 USC not included in this Action can be found in a prior Action.
This Office Action will be in response to applicant's arguments, filed 5/4/04.
The rejections of record can be found in the previous Office Actions.

Applicant's arguments and the examiner's rebuttal are essentially the same of record.

Given that applicant has argued that claim 73, drawn to methods for treating "restenosis" stands or falls on its own.

Newly added reference has been added to add further evidence to the references of record that the prior art renders such claims drawn to method for treating restenosis in a mammal to which a vessel-corrective technique is administered, encompassed by instant claim 73.

In addition, a New Grounds of Rejection has been set forth herein with respect to the claimed recitation of "another molecule" with respect to the chimeric PSGL constructs employed in the claimed methods.

3. The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 40-41, 49-52, 59-60 and 73 are rejected under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed.

There is insufficient written description encompassing "and another molecule" because the relevant identifying characteristics such as structure of other physical and/or chemical characteristics of said "molecule", are not set forth in the specification as filed, commensurate in scope with the claimed invention.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016.

One cannot describe what one has not conceived. See Fiddes v. Baird, 30 USPQ2d 1481, 1483. In Fiddes v. Baird, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence. Thus, the specification failed to describe these sequences. The Court further elaborated that generic statements are not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function. Finally, the Court indicated that while applicants are not required to disclose every species encompassed within a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, defined by nucleotide sequence, falling within the scope of the genus, See The Regents of the University of California v. Eli Lilly and Company, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

Page 9, lines 1-9, of the instant specification only discloses soluble forms of P-selectin or ligand including chimeric constructs between at least a portion of P-selectin or ligand and "other molecules". It is noted that the specification discloses that soluble forms of PSGL are described in Sako et al. (Cell 75: 1179-1186, 1993).

However, there appears insufficient written description as to structure as well as function of said "other molecules" in the specification as filed.

Applicant is relying upon certain biological activities of the entire chimeric construct and the structure of the P-selectin ligand element of the chimeric construct to support the broad genus of "and another molecule". The instant specification does not provide sufficient written description as to the structural features of said "another molecule" employed in the claimd chimeric constructs as currently encompassed by the claims. Also, the specification does not provide for the correlation between the chemical structure and the function of the genus of "another molecules", currently encompassed by the claimed invention. It has been well known that minor structural differences even among structurally related compounds or compositions can result in substantially different biology, expression and activities. The specification as filed does not provide sufficient written description either for structurally related or unrelated "another molecules" encompassed by the claimed invention.

A person of skill in the art would not know which "another molecules" are essential or non-essential to the use of the chimeric constructs in the claimed methods based upon the disclosure in the specification as filed

Mere idea or function is insufficient for written description; isolation and characterization at a minimum are required

The instant claims do not provide sufficient structural and functional characteristics coupled with a known or disclosed correlation between function and structure to support the genus of "another molecule" in the chimeric PSGL constructs employed in the claimed methods. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus of "another molecule", the specification does not provide sufficient written description for the genus of "another molecule" currently claimed.

The Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement make clear that if a claimed genus does not show actual reduction to practice for a representative number of species; then the Requirement may be alternatively met by reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001, see especially page 1106 column 3).

In the absence of structural characteristics that are shared by members of the genus of "another molecules"; one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, applicant was not in possession of the claimed genus. See University of California v. Eli Lilly and Co. 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997).

Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

"Adequate written description requires a precise definition, such as by structure, formula, chemical name or physical properties, not a mere wish or plan for obtaining the claimed chemical invention." Id. at 1566, 43 USPQ2d at 1404 (quoting Fiers, 984 F.2d at 1171, 25 USPQ2d at 1606). Also see Enzo-Biochem v. Gen-Probe 01-1230 (CAFC 2002).

Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.)

5. Claims 40-41, 49-52, 59-60 and 73 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Cummings et al. (U.S. Patent No. 6,309,639) in view of Tedder et al. (U.S. Patent No. 5,834,425), Coller et al. (U.S. Patent No. 5,976,532) and Sluiter et al. (J. Cardiovascular Pharmacology 22 (Suppl. 4): S37-S44, 1993).

Applicant's arguments in conjunction with the 1.131 declaration under 37 C.F.R. § 1.131, filed 5/4/04, have been fully considered but are not found convincing essentially for the reasons of record.

Applicant's arguments, filed 5/4/04, have been fully considered but are not found convincing essentially for the reasons of record.

Applicant's arguments and the examiner's rebuttal are essentially the same of record and reiterated herein for applicant's convenience.

Again, applicant asserts that the enclosed Declaration by the co-inventors demonstrates that the conception of the instant invention occurred as early as 1988 and that an actual reduction to practice occurred as early as 9/13/93. The time period between 11/16/92 and 9/13/93 was consumed by the development of a knockout mouse model for atherosclerosis and the testing of the mouse model to verify the inventive concept. It is noted that the conclusion of the results of the experiment were collected and analyzed on or about 5/6/94.

Applicant's rely on the statement: " Macrophages eat bits of activated platelets. ELAM-1 = Padgem. Do monocytes bind to Padgem on platelets. Padgem is an opsonizing agent to get rid of debris of platelets." Applicant assert their conception of a functional relationship between E-selectin and P-selectin, and that P-selectin mediates the binding of platelets to macrophages (leukocytes implicated in atheroclerosis).

Applicant relied upon the preparing a P-selectin knock-out mouse to study the role of P-selectin in atherosclerosis by feeding the P-selectin deficient mice with a lipid diet. The results of this study demonstrate a reduction in the size of atherosclerotic lesions in P-selectin deficient mice.

Applicant assert that based upon these results that inhibitors of P-selectin/ligand binding and/or E-selectin/ligand binding would be useful for the treatment or inhibition of atherosclerosis, constituting an actual reduction to practice the claimed invention.

The evidence, submitted is insufficient to establish a reduction to practice of the invention in this country prior to the effective date of the prior art.

The 37 CFR 1.131 declaration must establish possession of either the whole invention claimed or something falling within the claim in the sense that the claims as a whole reads on it. In re Tanczyn 146 USPQ 298 (CCPA 1965). See MPEP 715.02.

Applicant has not overcome the prior art rejection by showing that the differences between the claimed invention and the showing under 37 CFR 1.131 would have been obvious to one of ordinary skill in the art, in view of applicant's 37 CFR 1.131 evidence, prior to the effective date of the references(s) or the activity.

The test is whether the facts set out in the affidavit are such as would persuade one skilled in the art that the application possessed so much of the invention as is shown in the references. In re Schaub 190 USPQ 324 (CCPA 1976). See MPEP 715.03.

Applicant's evidence of conception and diligence does not address the critical elements of the instant claims which are drawn to a method of treating restenosis in a mammal to which a vessel-corrective techniques is administered comprising performing a vessel-corrective technique and administering PSGL-1.

There is insufficient evidence the ordinary artisan would have taken applicant statement: " Macrophages eat bits of activated platelets. ELAM-1 = Padgem. Do monocytes bind to Padgem on platelets. Padgem is an opsonizing agent to get rid of debris of platelets." to establish possession of treating restenosis in a mammal to which a vessel-corrective techniques is administered comprising performing a vessel-corrective technique and administering PSGL-1.

Similarly there is insufficient evidence the ordinary artisan would have taken applicant preparation of a P-selectin knock-out mouse to study the role of P-selectin in atherosclerosis by feeding the P-selectin deficient mice with a lipid diet to establish possession of treating restenosis in a mammal to which a vessel-corrective techniques is administered comprising performing a vessel-corrective technique and administering PSGL-1.

Further, it is noted that applicant's evidence relies upon experimental animals serves as model systems to selectively investigate different steps of the injury cascade providing specific insights into key mechanisms operating in diseases. While applicant's studies with a P-selectin knockout mouse may have provided insights into the role of P-selectin to atherosclerosis, there is insufficient evidence and correlation of establishing possession of treating restenosis in a mammal to which a vessel-corrective techniques is administered comprising performing a vessel-corrective technique and administering PSGL-1, particularly given the absence of any disclosure of treating restenosis in a mammal to which a vessel-corrective techniques is administered comprising performing a vessel-corrective technique and administering PSGL-1 in applicant's 131 Declaration and Exhibits.

Also, applicant has not provided objective evidence that applicant was in possession of PSGL-1 itself as well as its use as a therapeutic agent in treating restenosis prior to the disclosure of the prior art. Applicant's reliance on a generic concept of a possible role of P-selectin in atherosclerosis and subsequent findings in an experimental animal model does not support the use of PSGL-1 in treating restenosis.

Absent a clear support or facts are establishing applicant's assertions of conception and diligence (and reduction to practice or subsequent reduction to practice) before the prior art, applicant's arguments are not found persuasive and the rejection is maintained for the reasons of record.

Sluiter et al. has been provided to add further evidence that the ordinary artisan would have targeted the inhibition of P-selectin-mediated events in therapeutic strategies of inhibiting leukocyte adhesion receptors to alleviate tissue damage in cardiovascular diseases (see entire document, including Figure 1 and Table 1), including those patients suffering from heart attack, atherosclerosis and coronary restenosis (see Concluding Remarks on page S42).

Applicant asserts that Cummings et al. is directed to treating the inflammatory conditions resulting from the rupture of atherosclerotic lesions or plaque occurring which after the disease (atherosclerosis) has progessed to its end stages (see column 19, lines 57-64), which is distinct from the claimed methods directed to preventing the formation or growth of atherosclerotic lesions (i.e. conditions leading to the development of atherosclerosis).

However, the combination of references does provide sufficient motivation and expectation of success in providing chimeric PSGL-1 to treat various disorders and conditions associated with platelet-leukocyte interactions including atherosclerosis and ischemia, myocardial infarction and reperfusion injury, encompassed by the claimed methods. For example, see Clinical Applications on columns 18-22 and Claims of Cummings et al. Cummings et al. also teach that both acute and chronic disorders are targeted therapies (see column 18, paragraph 5) as well as the pathological situations arising from issue damage resulting from leukocytes associated with ischemia and reperfusion as well as clinical cardiology (see columns 18, paragraphs 6-7 to column 19, paragraph 1).

Given the prior art teachings supporting methods of treating artherosclerosis as well as treating patients undergoing vessel-corrective techniques, decreasing the formation or growth of atherosclerotic lesions as well as treating or inhibiting atherosclerosis would have been an expected or intrinsic property of treating patients undergoing vessel-corrective techniques with PSGL-1.

Applicant acknowledges that Tedder et al. discloses that chimeric peptides can be formed from different selectins but asserts that applicant is claiming a method of using certain chimeric molecules to treat atherosclerosis and restenosis..

As pointed out previously, Tedder et al. teach the art known generation and use of chimeric peptides combining ligand binding portions of selecting based inhibitory therapeutics, including those based upon P-selectin, with other molecules such as immunoglobulin to increase serum half-life or avidity of the therapeutic agent to block platelet or leukocyte-mediated inflammation (see entire document, including Use on columns 10-14). Similar to Cummings et al. and art known practice at the time the invention was made, Tedder et al. teach combination therapy (see column 13, paragraph 1).

Given the art known practice and desire to increase the avidity and/or half-life of therapeutics in general, including selectin-mediated inhibitors, as taught by Tedder et al., one of ordinary skill in the art would have been motivated to modify the PSGL-1 and fragments thereof taught by Cummings et al. By making chimeric constructs thereof in the treatment of cardiovascular disorders.

Applicant asserts that there is no motivation to combine Coller et al. with Cummings et al. because Cummings et al. does not mention surgical procedures or chimeric molecules and Cummings et al. / Tedder et al. are directed to inflammatory conditions which are not discussed in Coller et al.

Again, Cummings et al. teach the clinical applications, including atherosclerosis and ischemia, myocardial infarction and reperfusion injury, by inhibiting platelet-leukocyte interactions with PSGL-1 and fragments thereof (see entire document, including Clinical Applications on columns 18-22 and Claims). Cummings et al. teach that the therapeutic use that reduce leukocyte adherence in ischemic myocardium can significantly enhance the therapy efficacy of thrombolytic agents (see column 18, paragraph 7).

Also, as pointed out previously, Coller et al. teach the art known vessel-corrective techniques at the time the invention was made in the treatment of cardiovascular disorders such as atherosclerosis and reocclusion, including angioplasty, atherectomy and coronary bypass surgery (see Background of the Invention on column 1 and Utility of Platelet-specific Chimeric Immunoglobulin on columns 5-7). In teaching the use of an inhibitor of platelet aggregation and thrombus formation associated with such conditions, Coller et al. teach the art known use of combination therapy with other drugs such as thrombolytic agents and that the amounts administered before, along with or subsequent to treatment will depend on a variety of factors and clinical symptoms known to the ordinary artisan at the time the invention was made (see column 6, paragraphs 2-3). Coller et al. teach that antibodies reactive with platelets, including antibodies that bind GMP-140 (i.e. P-selectin) can be used (see column 3, paragraph 3). Therefore, the prior art does teach targeting P-selectin in the context of vessel-corrective procedures.

In contrast to applicant's assertions, Cummings et al. and Coller et al. are drawn to the same or similar methods of inhibiting platelet-leukocyte / endothelial interactions for various clinical applications, including atherosclerosis and ischemia, myocardial infarction and reperfusion injury as well as cardiovascular disorders such as atherosclerosis and restenosis, including angioplasty, atherectomy and coronary bypass surgery.

Given the art known practice of combination therapy, as taught by Cummings et al., Tedder et al. and Coller et al. as well as the art known practice of vessel-occlusive techniques to treat atherosclerosis and restenosis, as taught by Coller et al., one of ordinary skill in the art would have been motivated to administer the PSGL-1 and fragments thereof, as taught by Cummings et al. in various vessel-occlusive techniques given its properties of inhibiting platelet-leukocyte interactions for various clinical applications, including atherosclerosis and ischemia, myocardial infarction and reperfusion injury, as taught by Cummings et al. with an expectation of success.

Given the art known practice of modes of administrations and dosing depending on a variety of factors and clinical symptoms known to the ordinary artisan at the time the invention was made, as taught by Coller et al. In cardiovascular diseases, the claimed limitations were met or would have been obvious variants in meeting the needs of the patients in order to achieve a therapeutic effect depending on the symptom at the time the invention was made.

From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

One cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. In re Keller , 642 F.2d 413, 208 USPQ 871 (CCPA 1981); In re Merck & Co., Inc. , 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). See MPEP 2145.

Applicant's arguments have not been found persuasive.

6. No claim is allowed.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (571) 272-0844. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841.

The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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